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Original Article

Two dimensional speckle tracking echocardiography in detection of subclinical left ventricular systolic dysfunction in patients with severe aortic stenosis

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ABSTRACT

Introduction: Subclinical left ventricular (LV) systolic dysfunction may develop in patients with severe aortic stenosis (AS) despite normal LV ejection fraction (EF%).

The aim of the study: To evaluate the role of two dimensional (2D) speckle tracking echocardiography (STE) in detection of subclinical LV systolic dysfunction in patients with severe AS.

Patients and method: The study included 50 patients with severe AS (mean age: 45 ± 9 years) and 30 age-matched healthy individuals (mean age 43 ± 7 years. Conventional echocardiographic parameters used for the assessment of AS severity were measures and 2D Speckle tracking imaging of the peak systolic strain curves of the Inferior septum and lateral wall in the apical four-chamber view (4C-PLS), the Inferior and anterior wall was in the apical two chamber view (2C-PLS), and the infero lateral and anterior septum in the apical three-chamber view (3C-PLS) were obtained. Left ventricular global longitudinal systolic strain (LV-GLS) was calculated by averaging the peak systolic values of the 6 LV walls.

Results: LV-GLS was significantly reduced in patients with AS compared to controls (<0.001) and negatively correlated with left ventricular mass index (LVMI) ($r = -0.47$, $p = 0.01$) irrespective of EF%, maximum velocity, peak pressure gradient and mean pressure gradient across the aortic valve and the aortic valve area.

Conclusion: Patients with severe AS have evidence of subclinical LV systolic dysfunction despite preserved EF%. 2D speckle tracking appears to be useful in detection of subclinical LV dysfunction in patients with AS.

1. Introduction

Aortic stenosis (AS) is one of the common valvular heart diseases, mostly caused by rheumatic fever. In patients with severe AS, left ventricular hypertrophy (LVH) and elevated left ventricular (LV) filling pressure, impair the coronary flow reserve and renders the LV myocardium susceptible to ischemia, especially the longitudinal fibers of the

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subendocardial layer. Thus, longitudinal shortening is the first measurement to be compromised in patients with AS.[1]

Conventional echocardiography is appropriate to detect significant LV dysfunction but not subclinical dysfunction.[2] Two-dimensional (2D) speckle-tracking echocardiography (STE) allows an angle independent evaluation of the myocardial strain, providing comprehensive information on LV myocardial contractility and is superior in detecting subtle deteriorations of contractility.[3]

1.1. *Aim of the study*

To evaluate the role of speckle tracking echocardiography in detection of subclinical LV systolic dysfunction in patients with severe AS.

2. Patients and methods

The study included 50 patients with severe AS due to congenital and rheumatic aortic valve disease (mean age: 37 ± 8 years) and 30 age-matched healthy individuals (mean age 36 ± 6 years). The study was approved by the ethical committee of the hospital and all included subjects have consented to be enrolled in this study.

2.1. *Exclusion criteria*

We excluded patients with concomitant moderate to severe aortic regurgitation (AR), subvalvular AS, mitral valve disease, coronary artery disease (CAD), patients with LV systolic dysfunction (ejection fraction (EF %) <50%) and patients with cardiac rhythm disturbances such as atrial fibrillation or artificial pacing.

Each person included in the study was subjected to:

1. **Careful history taking and thorough physical examination**.
2. **Standard twelve-lead electrocardiogram (12-lead ECG):** For assessment of cardiac rhythm and features suggesting of chamber enlargement and CAD.
3. **Basic echocardiographic measurements:** Echocardiography was performed using an Aplio 400, Toshiba, Japan ultrasonographic machine with an M4S transducer. The patients were monitored through a single-lead electrocardiogram. The left atrial diameter, left ventricular end-systolic and end-diastolic diameters, left ventricular fractional shortening percentage (FS%), the thickness of the interventricular septum (IVS), and the posterior wall (PW) were measured according to the recommendations of the American Society of Echocardiography. The LV EF% was calculated by Simpson's biplane method of discs. The left ventricular mass (LVM) was calculated using the formula proposed by Devereux et al and corrected by the body surface area to derive LV mass index (LVMI).[4] LVMI <102 g/m^2 for men and <88 g/m^2 for women indicate normal LV mass, LVMI 103–116 g/m^2 for men and 89–100 g/m^2 for women indicate mild LVH, LVMI 117–130 g/m^2 for men and 101–112 g/m^2 for women indicate moderate LVH and LVMI >130 g/m^2 for men and >112 g/m^2 for women indicate severe LVH.[5] Doppler assessment of AS included the measurement of the maximum velocity across aortic valve (V. Max), maximum aortic valve pressure gradient (PG) and mean aortic valve pressure gradient (MG). Aortic valve area (AVA) was calculated by means of the continuity equation and assessment of the severity of AS was based on a variety of hemodynamic data, using maximum velocity across aortic valve V. Max, MG and AVA and severe AS was diagnosed when V. Max > 4 m/sec, MG > 40 mmHg or AVA < 1.0 cm^2.[6]
4. **Measurement of the speckle tracking peak systolic strain:** 2D echocardiography images (transmit/receive 1.9/4.0 MHz) were obtained from LV apical LAX, 4C, and 2C views with frame rates of 30–90 frames/s. Digital data were stored and analyzed off-line. LV endocardial surface was traced manually, and the speckle tracking width was modified so as to cover the whole LV wall thickness to obtain curves for peak longitudinal strain of the Inferior septum and lateral wall in the apical four-chamber view (4C-PLS), the Inferior and anterior wall was in the apical two chamber view (2C-PLS), and the infero lateral and anterior septum in the apical three-chamber view (3C-PLS). Left ventricular global longitudinal systolic strain (LV-GLS) was calculated by averaging the peak systolic values of the 6 LV walls. As shown in Fig. 1.

All the echocardiographic studies were performed by one echocardiographer and for intra-observer variability, a sample of 2D strain was randomly selected and examined by the same observer in two different days and intra-class correlation coefficients for the same observer were calculated.

3. Statistical analysis

Collected data were computerized and analyzed using Statistical Package for Social Science (SPSS) version 16. Descriptive statistics were used to describe variables; percent, proportion for qualitative variables. Mean SD and range for Quantitative variables. Student's *t*-test was used to compare the normally distributed continuous variable between the patients with aortic valve stenosis and the healthy control group. Fisher-exact test and Chi-square test were used to compare categorical variables. *p* values with significance of less than 5% were considered statistically significant. For all statistical tests, a *p* value less than 0.05 was used to indicate significance.

4. Results

4.1. *Demographic and conventional echocardiographic characteristic*

There was no significant difference between, gender, heart rate, systolic and diastolic blood pressure, LVESD, LVEDD, LVESV LVEDV, EF% and FS% in patients with AS compared to control group ($p > 0.05$), There was highly significant difference in IVS and PW thickness, LVMI and left atrium diameter in patients with AS compared to control group ($p < 0.001$). In patients with AS; 14 patients had congenital bicuspid aortic

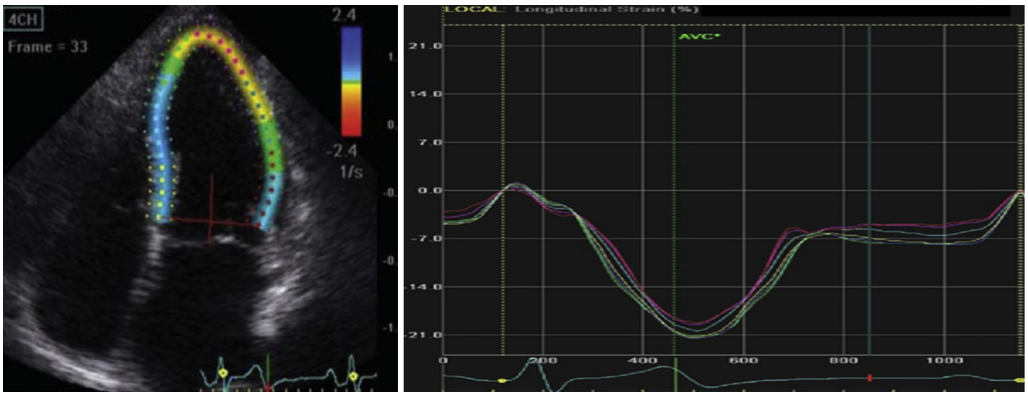

Fig. 1 – Apical 4 chambers longitudinal strain curves in a healthy subject.

valve, 23 patients had concomitant mild AR, V. Max (495 ± 50 cm/s), PG (88 ± 13 mmHg), MG (57 ± 11 mmHg), mean AVA (0.81 ± 0.09 cm^2), mild-moderately increased LVMI in 40% of patients and markedly increased LVMI in 60% of patients (118 ± 10 g/m^2 vs., 147 ± 15 g/m^2, $p < 0.001$). As shown in Table 1.

4.2. *2D strain measurements*

Peak longitudinal systolic strain was very significantly reduced in patients with AS as compared to the control group (Inferior septum wall, −12.9 ± 3.6 vs. −19.3 ± 2.5; lateral wall, −12.5 ± 3.5 vs. −18.7 ± 3.2; inferior wall, −13.7 ± 3.9 vs. −19.2 ± 2.8; anterior wall, −12.1 ± 3.4 vs. −19.8 ± 2.1, infero-lateral wall, −12.4 ± 3.7 vs. −18.9 ± 3.7; anterior septum wall, −12.8 ± 3.9 vs. −20.1 ± 1.9; and LV-GLS, −12.7 ± 3.6 vs. −19.3 ± 2.7; $p < 0.001$ for all). As shown in Table 2.

LVMI was mild-moderately increased in 40% of patients with AS and markedly increased in 60% of patients with AS (118 ± 10 g/m^2 vs. 147 ± 15, g/m^2 $p < 0.001$), patients with marked left ventricular hypertrophy had significantly reduced peak longitudinal systolic strain compared to patients with mild-moderate left ventricular hypertrophy (Inferior septum wall, −10.3 ± 0.9 vs. − 12.2 ± 2.4; lateral wall, −09.9 ± 0.8 vs. −11.8 ± 3.2; inferior wall, −10.7 ± 0.6 vs. −12.1 ± 2.7; anterior wall, −09.9 ± 1.2 vs. −11.7 ± 2.5, infero-lateral wall, −09.6 ± 0.7 vs. −11.5 ± 2.1; anterior septum wall, −10.1 ± 1.3 vs. −12.4 ± 2.8; and LV-GLS, −10.0 ± 0.9 vs. −11.9 ± 2.6; $p < 0.001$ for all). As shown in Table 3.

A Pearson correlate revealed significant negative correlation between LV-GLS and LVMI ($r = -0.47$, $p = 0.01$), no significant correlation between LV-GLS with EF% ($r = 0.16$, $p = 0.19$), V. Max ($r = -0.05$, $p = 0.78$), PG ($r = -0.12$, $p = 0.41$), MG ($r = -0.09$, $p = 0.56$) and AVA ($r = 0.13$, $p = 0.25$). As shown in Table 4.

The intra-class correlations for intra-observer variability were also good for LV-GLS (0.94, 95% CI 0.79–0.97).

Table 1 – Clinical and echocardiographic features of the study groups.

	Control	AS	*p* value
Age, years	43 ± 7	45 ± 9	0.3
Male/Female	20/10	30/20	NS
Heart Rate, bpm	73 ± 6	75 ± 7	0.19
SBP, mmHg	125 ± 9	123 ± 7	0.27
DBP, mmHg	80 ± 7	78 ± 5	0.14
IVS dimension, cm	0.85 ± 0.12	1.46 ± 0.12	<0.001
PWS dimension, cm	0.87 ± 0.09	1.39 ± 0.09	<0.001
LV end-diastolic diameter, cm	4.82 ± 0.30	4.68 ± 0.33	0.06
LV end-systolic diameter, cm	3.17 ± 0.18	3.22 ± 0.07	0.74
LV end-diastolic volume, ml	103 ± 18	101 ± 16	0.06
LV end-systolic volume, ml	34 ± 12	35 ± 14	0.74
EF, %	65 ± 8	62 ± 6	0.06
FS, %	34 ± 4	31 ± 8	0.06
LA diameter, cm	3.65 ± 0.22	3.82 ± 0.15	<0.001
V. Max, cm/sec	–	495 ± 50	–
PG, mm Hg	–	88 ± 13	–
MG, mm Hg	–	57 ± 11	–
AVA, cm^2	–	0.81 ± 0.09	–

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; IVS, interventricular septum; PWS, posterior wall thickness; LVMI, left ventricular mass index; BSA, body surface area; LV, left ventricle; EF; ejection fraction, S, fractional shortening, V. Max, maximum velocity across aortic valve; PG, trans-aortic peak systolic gradient; MG, trans-aortic mean systolic gradient; AVA, aortic valve area.

5. Discussion

In patients with severe AS, LV systolic dysfunction on the basis of EF% is a class I indication for aortic valve replacement

Table 2 – Speckle tracking LV peak longitudinal systolic strain of the study groups.

	Control	AS	*p* value
PLS-Inferior septum, %	−19.3 ± 2.5	−12.9 ± 3.6	<0.001
PLS-Lateral wall, %	−18.7 ± 3.2	−12.5 ± 3.5	<0.001
PLS-Inferior wall, %	−19.2 ± 2.8	−13.7 ± 3.9	<0.001
PLS-Anterior wall, %	−19.8 ± 2.1	−12.1 ± 3.4	<0.001
PLS-Infero-lateral, %	−18.9 ± 3.7	−12.4 ± 3.7	<0.001
PLS-Anterior septum, %	−20.1 ± 1.9	−12.8 ± 3.9	<0.001
LV-GLS, %	−19.3 ± 2.7	−12.7 ± 3.6	<0.001

Abbreviations: AS, aortic stenosis; PLS, peak longitudinal systolic strain; GLS-LV, left ventricular global longitudinal systolic strain.

Table 3 – Comparison between LV peak longitudinal systolic strain in patients with AS with mild-moderate and marked LVH.

	Mild-moderate LVH	Marked LVH	*p* Value
PLS-Inferior septum, %	−12.2 ± 2.4	−10.3 ± 0.9	<0.001
PLS-Lateral wall, %	−11.8 ± 3.2	−09.9 ± 0.8	<0.001
PLS-Inferior wall, %	−12.1 ± 2.7	−10.7 ± 0.6	<0.001
PLS-Anterior wall, %	−11.7 ± 2.5	−09.9 ± 1.2	<0.001
PLS-Infero-lateral, %	−11.5 ± 2.1	−09.6 ± 0.7	<0.001
PLS-Anterior septum, %	−12.4 ± 2.8	−10.1 ± 1.3	<0.001
LV-GLS, %	−11.9 ± 2.6	−10.0 ± 0.9	<0.001

Abbreviations: LVH; left ventricular hypertrophy; PLS, peak longitudinal systolic strain; LV-GLS, left ventricular global longitudinal systolic strain.

(AVR) irrespective of the presence or absence of symptoms, and EF% is the only parameter of LV systolic function included in the recent European guidelines.[6] Consequently detection of subtle LV contractile dysfunction at an early subclinical stage allows earlier surgical intervention by aortic valve replacement (AVR) to prevent irreversible LV deterioration.[7] Newer echocardiographic methods like STE are sensitive marker for assessment of regional and global LV systolic function and may allow earlier detection of LV systolic dysfunction in subjects with severe AS and preserved EF%.[8]

Our results showed significantly reduced peak longitudinal systolic strain in patients with AS compared to the control group (Inferior septum wall, −12.9 ± 3.6 vs. −19.3 ± 2.5; lateral wall, −12.5 ± 3.5 vs. −18.7 ± 3.2; inferior wall, −13.7 ± 3.9 vs. −19.2 ± 2.8; anterior wall, −12.1 ± 3.4 vs. −19.8 ± 2.1, infero-lateral wall, −12.4 ± 3.7 vs. −18.9 ± 3.7; anterior septum wall, −12.8 ± 3.9 vs. −20.1 ± 1.9; and LV-GLS, −12.7 ± 3.6 vs. −19.3 ± 2.7; $p < 0.001$ for all). Our results came in agreement with **Kjetil et al**[9] who found significantly lower LV longitudinal peak systolic strain in patients with AS compared with controls (−16.6 ± 2.7% vs. −17.9 ± 2.0%, $p < 0.05$). **Erwan et al**[10] found that patients with AS have reduced longitudinal myocardial function at rest and at peak exercise compared to normal control (−15.4 ± 4.0 vs. −20.2 ± 2.7 and −16.5 ± 4.9 vs. −25.0 ± 3.7, $p < 0.0001$ for both). **Betül et al**[11] found significantly lower LV longitudinal peak systolic strain in patients with AS compared to controls (−9.66 ± 1.29% to −17.60 ± 2.18%, $p < 0.0001$). **Delgado et al**[12] found that patients with severe AS and preserved EF% had impaired GLS measured by 2D-STE. **Kearney et al**[13] found significantly reduced GLS in subjects with moderate and severe AS despite normal EF% ($p < 0.001$). **Aleksander et al**[14] found that 38% of patients with AS and normal EF% had abnormally low LV-GLS (−12.2 ± 2.4%). **Adam et al**[15] reported that despite of similar EF% in the AS and the control group (59.6 ± 7.0 vs. 58.0 ± 6.6%, $p = 0.24$), patients with AS had significantly lower peak systolic longitudinal (−8.7 ± 2.4 vs. −13.2 ± 2.5%, $p < 0.001$).

Table 4 – Correlations between LV-GLS and echocardiographic parameters in patients with AS.

	LV-GLS	
	r Value	*p* Value
LVMI	−0.47	0.01
EF%	0.16	0.19
V. Max	−0.05	0.78
PG	−0.12	0.41
MG	−0.09	0.56
AVA	0.13	0.25

Abbreviations: LV-GLS, left ventricular global longitudinal systolic strain; LVMI, left ventricular mass index; EF, ejection fraction; V. Max, maximum velocity across aortic valve; PG, trans-aortic peak systolic gradient; MG, trans-aortic mean systolic gradient; AVA, aortic valve area.

Impairment in the global longitudinal systolic strain observed in our study might be due to the increase in LV subendocardial wall stress, ischemia and fibrosis. **Seung et al**[16] reported that patients with severe AS and LV systolic dysfunction had some degree of late gadolinium enhancement in the LV myocardium. **Frank et al**[17] assessed the relation between myocardial functions and fibrosis in patients with severe AS and found evidence of impairment of the LV longitudinal systolic strain with increasing degrees of myocardial fibrosis. These findings support a general cascade of severe aortic valve stenosis leading to LV hypertrophy and myocardial fibrosis.

Our study revealed that, increased LV mass was associated with reduced longitudinal myocardial systolic strain. Patients with marked LVH had lower LV-GLS compared to patients with mild-moderate LVH (Inferior septum wall, −10.3 ± 0.9 vs. −12.2 ± 2.4; lateral wall, −09.9 ± 0.8 vs. −11.8 ± 3.2; inferior wall, −10.7 ± 0.6 vs. −12.1 ± 2.7; anterior wall, −09.9 ± 1.2 vs. −11.7 ± 2.5, infero-lateral wall, −09.6 ± 0.7 vs. −11.5 ± 2.1; anterior septum wall, −10.1 ± 1.3 vs. −12.4 ± 2.8; and LV-GLS, −10.0 ± 0.9 vs. −11.9 ± 2.6; $p<<0.001$ for all). LV-GLS was independently associated with the extent of LVMI ($r = -0.47$, $p = 0.01$) irrespective of EF% ($r = 0.16$, $p = 0.19$), V. Max ($r = -0.05$, $p = 0.78$), PG ($r = -0.12$, $p = 0.41$), MG ($r = -0.09$, $p = 0.56$) and AVA ($r = 0.13$, $p = 0.25$). Our results came in agreement with **Wilfried et al**[7] who found lower GLS in patients with AS compared to control group (−15.2 ± 3.6 vs. −19.5 ± 2.7, $p < 0.001$) and the proportion of GLS impairment depends on the extent of LVH ($r = 0.6$, $p < 0.001$). In addition, **Cramariuc et al**[18] found that LVH and concentric geometry were independently associated with lower longitudinal myocardial strain irrespective of the severity of AS and EF% ($r > 0.40$). On the other hand, **Jutta et al**[19] observed that GLS was not related to degree of LVH, EF% or AVA. In addition, **Erwan et al**[10] found no correlation between the global longitudinal function and the degree of LVH.

6. Conclusion

Patients with AS and preserved EF% had lower LV-GLS. 2D speckle tracking appears to be useful in detection of subclinical LV dysfunction in patients with AS.

7. Study limitations

The potential limitation of the present study is the relatively small sample size so the results may not be generalized. As

only standard apical images were obtained, we could only measure longitudinal strain, so neither circumferential nor radial strain analysis could be carried out.

Conflicts of interest

The author has none to declare.

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